#16
Dice
6/18/02

Atty. Doc. No.: PXE-007.US
(9400-0002.01)
USSN: CPA of 09/464,795

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Contag and Zhang

Serial No.: CPA of 09/464,795 Art Unit: 1632

Filing Date: 16 December 1999 Examiner: R. Shukla

Title: NON-INVASIVE EVALUATION OF PHYSIOLOGICAL RESPONSE IN A MAMMAL

Reconsidered
RN 8/13/02

DECLARATION OF DAVID B. WEST, PhD
PURSUANT TO 37 C.F.R. §1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, David B. West, hereby declare as follows:

1. I received my Bachelors of Science Degree in Biology from the University of Washington in 1977; and my Doctorate of Philosophy Degree in Physiology and Psychology in 1984 from the University of Washington.

2. I am currently the Senior Director of Preclinical Reserach at Xenogen Corporation and have held this position since April 9, 2001. Before joining Xenogen, I worked as Director of Mouse Genetics at Pfizer, Incorporated. Additional details regarding my background and qualifications can be found in the accompanying copy of my *Curriculum Vitae.*

3. I have reviewed pending Patent Application Serial No. 09/464,795 for "NON-INVASIVE EVALUATION OF PHYSIOLOGICAL RESPONSE IN A MAMMAL " by Contag and Zhang, (hereinafter "the specification") including pending claims 38, 40, 41, 43, 45, 46, 49 and 65-68. I have also reviewed (1) the Final Office Action dated September 13, 2001; (2) Cameron (1997) *Molecular Biotechnology* 7:253-

265; and (3) Cui et al. (1994) *Transgenic Research* 3:182-194. Therefore, I am familiar with the issues raised by the Examiner.

4. I understand that pending claims 38, 40, 41, 43, 45, 46, 49, and 65-68 are directed to transgenic mice and methods of using such mice. In particular, I understand that the transgenic mice comprise a panel of expression cassettes. Each expression cassette of this panel includes a control element from a stress-inducible gene operably linked to a sequence encoding a light-generating protein. Similarly, I understand that there are methods of using such mice to determine the effect of an analyte on gene expression.

5. In December of 1999, when the specification was filed, a typical scientist working the field of transgenic animals had a Ph.D. in the Biological or Chemical Sciences and two to five years of relevant experience. I will call such a person a "typical scientist."

6. When the specification was filed, it clearly conveyed to a typical scientist that the inventors had in their possession the invention of the claims (as set forth in paragraph 4, above). By "in their possession," I mean that the inventors contemplated transgenic mice comprising a panel of expression cassettes, wherein the panel comprises at least two different expression cassettes, each having a different stress-inducible control element operably linked to sequence encoding a light-generating polypeptide, and that they had, using the specification and information available to a typical scientist, a practical way of making and using such transgenic mice. Thus, I believe that a typical scientist would have understood the specification clearly described all of the various aspects of the claims and enabled a typical scientist to make and use the invention as set forth in the pending claims. I base this belief on the facts set forth below.

7. First, at the time the specification was filed, it was widely known how to construct expression cassettes generally. With regard to expression vectors comprising control elements from stress-inducible promoters operably linked to a sequence encoding a light-generating polypeptide, such methods are described in detail in the specification, for example, in Section 3.1.0 of the specification. Therefore, it is my opinion that construction of a panel of expression cassettes as set forth in the claims would have been routine to a typical scientist working in this area in view of the teachings of the specification.

8. Second, it would have been clear to a typical scientist that the inventors had in their possession the various polynucleotide components of the expression cassettes. Control elements derived from stress-inducible genes were known and clearly set forth in the specification at the time of filing. (See, Section 3.1.1 starting on page 35

of the specification). Similarly, the specification clearly describes sequences encoding light-generating proteins. (See, Section 3.2.0 starting on page 58 of the specification). Thus, it is my opinion that light-generating polypeptide-encoding sequences operably linked to control elements derived from stress-inducible genes of the expression cassettes of the claims are fully described in the specification.

9. Third, it would have been plain to a typical scientist from the specification that the inventors were in possession of an operative way of making the claimed transgenic mice. The specification describes methods of making transgenic animals on page 59, line 28 to page 60, line 8 and in the references cited therein. At the time the application was originally filed, such methods were routine to the typical scientist. Indeed, methods of introducing multiple expression constructs, each with their own separate promoter, to create transgenic founders are described in the art. (See, *e.g.*, Jankowsky et al. (2001) *Biomol Eng* 17(6):157-165, copy of the Abstract attached hereto). Also routine at the time of filing were methods of assaying if a sequence from an expression cassette had been integrated into a host mouse's genome and, if so, where such integration occurred. Such assay methods include, but are not limited to, PCR, Northern and/or Southern blotting (for example of particular tissues) as well as *in situ* hybridization and/or imaging techniques.

10. Fourth, a typical scientist would have known that the inventors were in possession of operative methods of using these transgenic mice, for example, to determine the effect of an analyte. The evaluation of whole transgenic animals having light-reporter systems is described on line 29, page 60 through line 6, page 61 of the specification. It is also my opinion that applying these methods of evaluation to the claimed transgenic mice and methods of using these mice would have been routine to one working in this area in view of Applicants teachings.

11. It is further my opinion that one skilled in the art would understand from the specification that the claimed transgenic mice could be made using techniques described in the specification or known at the time of filing. (See, *e.g.*, page 59, line 28 to page 60, line 8). Further, the specification discusses how to prepare transgenic animals and how to performing imaging experiments on these animals, etc. Thus, I believe that, based on the application and level of skill in the art, one working in this field would be able to make and use the claimed transgenic mice.

12. It is further my opinion that Cameron and Cui are not relevant to the subject matter claimed in the application. Cameron is directed primarily to transgenic livestock. (See, Cameron, Abstract). Further, the issues raised in Cameron regarding poor levels of expression are not relevant to the claimed invention for a variety of

reasons. First, transgenic mice containing the claimed expression cassettes can be readily assayed for expression levels and only those animals exhibiting the desired expression levels can be used. (See, also, paragraph 9 above). Second, leaky expression is not a major issue in the practice of the present invention -- where the expression cassettes integrate is irrelevant so long as expression of the light-generating protein is inducible via a stress-inducible control element. (See, also, paragraph 9 above). For its part, Cui is not relevant to the claimed invention because it is not directed to the use of light-generating proteins as *in situ* reporters. (See, Cui, page 183). Thus, I believe that one working in this field would have no reason to apply this information to the claimed invention. Accordingly, I do not believe that Cameron or Cui to be relevant to the claimed invention.

13. Therefore, taken as whole, the specification unambiguously conveyed to a typical scientist that the inventors contemplated including a panel of expression cassettes in a transgenic mouse comprising the stress-inducible control element operably linked to light-generating polypeptide-encoding sequence as disclosed in the specification. The inventors also had in their possession an operative way of using these transgenic animals to evaluate the effect of analyte in a whole animal. In sum, based on the disclosure of the specification and the level of knowledge of a typical scientist regarding expression cassettes, transgenic animals and assays for integration available at the time of filing, I believe that the specification as filed clearly conveys that the applicants had invented the expression cassettes and methods as set forth in the claims.

14. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

May 8, 2002
Date

David B. West, Ph.D.

CURRICULUM VITAE

David B. West, Ph.D.

PERSONAL

Place of Birth: Pittsburgh, PA
Citizenship: United States
SSN: 536-56-5817

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Xenogen Corporation
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E-MAIL: david.west@xenogen.com

Visiting Scientist
Lawrence Berkeley National Laboratory
Berkeley, CA

Home Address:

5840 St. Paul Court
Oakland, CA 94618
TEL: 510-339-2912

EDUCATION

1983 — Ph.D. in Physiology/Psychology
University of Washington, Seattle, WA
Dissertation Title: Abnormal Perinatal and Infant Nutrition as a Cause of Obesity: Development of an Animal Model

1976 — B.S. Cellular and Molecular Biology,
Cum Laude and Phi Beta Kappa
University of Washington, Seattle, WA

PROFESSIONAL EXPERIENCE

April 2001 – Present	Sr. Director of Preclinical Research Xenogen Corporation Alameda, CA
June 2000 – Jan. 2001	Director of Mouse Genetics Pfizer Global Research and Development Alameda, CA
May 1998 – June 2000	Director of Mouse Genetics Parke-Davis Laboratory for Molecular Genetics Alameda, CA
June 1999 – Present	Visiting Scientist Lawrence Berkeley National Laboratory Department of Molecular Medicine
May 1998 - Present	Adjunct Professor Pennington Biomedical Research Center
Mar. 1997 - Mar. 1998	On 75% time Academic Leave Participated in start-up of gene/Networks, Inc. A biotechnology company.
Sept. 1996 - 1998	Professor, Pennington Biomedical Research Center and Adjunct Professor in School of Veterinary Medicine and School of Medicine, Louisiana State University
Feb. 1991 - 1996	Associate Professor Pennington Biomedical Research Center Louisiana State University
	Adjunct Associate Professor Department of Physiology School of Veterinary Medicine Louisiana State University
	Adjunct Associate Professor Department of Physiology Louisiana State University School of Medicine New Orleans, LA (Effective 1993)

1987 - Feb. 1991	Assistant Professor of Physiology and Internal Medicine Eastern Virginia Medical School Norfolk, VA Staff Scientist Veterans Administration Medical Center Hampton, VA
1986 - 1987	Adjunct Assistant Professor of Biology Vassar College Poughkeepsie, NY
1984 - 1986	Individual NIH Postdoctoral Fellow Sponsor: Greenwood, M.R.C. Vassar College Poughkeepsie, NY
1977 - 1983	NIH Predoctoral Fellow in the Departments of Physiology and Psychology University of Washington Seattle, WA

RELATED PROFESSIONAL EXPERIENCE

1984 - 1987	Writer, Medical Literature Review Corporation St. James, NY

RESEARCH FUNDING

March, 1998- February, 2002	National Institutes of Health RO1 #DK53393 An obesity locus on mouse chromosome 7 Estimated total direct costs for 4 years: $1,002,628 Approximately 40% of project subcontracted to Dr. Dabney Johnson, Oakridge National Laboratory
1994 - Sept, 2001	National Institutes of Health RO1 #DK45895 Metabolic and genetic markers for dietary obesity Current funding period September 1, 1997 - August 31, 2001 Estimated total direct costs for 4 years: $1,160,521
Jan, 1998 - Dec, 1999	National Cattleman's Beef Association Co-PI with James P. DeLany Effects of conjugated linoleic acid on metabolism in the mouse.

Estimated total direct costs for 1 year: $75,000

1991 - 1996 — National Institutes of Health R29 #DK44446
Nutrition and hypertension: Role of hyperinsulinemia

1991 - 1992 — Pew National Nutrition Program
Fellowship for Faculty Scholars in Nutrition

1989 - 1990 — Diabetes Center of Eastern Virginia
Grant in Aid.
Insulin resistance and dietary obesity: Role of altered renal function in the development of obesity-related hypertension

1987 - 1988 — Eastern Virginia Medical School
Institutional Research Grant
Obesity and Hypertension

1985 - 1988 — National Institutes of Health ROl #HD12637
Co-Principal Investigator with Greenwood, M.R.C.,
Nutrition and adipocyte growth and development

1985 - 1987 — Hoffmann-La Roche Inc.
Research Contract
Peptides and feeding behavior

1985 - 1987 — New York Heart Association
Grant-in-Aid
Co-Principal Investigator with Greenwood, M.R.C.,
Altered blood flow and metabolism in obese fa/fa rats

1984 - 1986 — National Institutes of Health
Individual Postdoctoral Fellowship #AMO7332
Early nutritional factors in the etiology of obesity

RESEARCH INTERESTS

Molecular genetics of obesity
Molecular genetics of complex disorders
Obesity and hypertension
Early nutrition in the etiology of obesity
Adipose tissue physiology and metabolism

ACADEMIC RESEARCH IN PROGRESS

NIH-funded: Genetic and metabolic basis of dietary obesity
Cloning an obesity gene on mouse chromosome 7

Other: Metabolic effects of conjugated linoleic acid

TEACHING EXPERIENCE

1987 - 1991 Eastern Virginia Medical School:
Physiology: Year 1 Medical Students

1984 - 1987 Vassar College:
Guest Lecturer, Endocrinology

Laboratory Instructor in Nutrition (Supervisor of a minimum of 3 independent students each year)
Guest Lecturer, Principles of Nutrition

University of Washington:
1982 Instructor, Surgical and Histological Techniques

1981 Teaching Assistant, Animal Learning Laboratory

1978 - 1980 Teaching Assistant, Surgical and Histological Techniques

TEACHING INTERESTS

Molecular Genetics
Nutrition
Physiology
Metabolism and Endocrinology

GRADUATE STUDENTS SUPERVISED

Gerald Thompson, Department of Kinesiology, Louisiana State University; Ph.D. awarded in July, 1996.
Dissertation: Post-exercise Hypotension in the Dog

Agatha Borne, DVM, Department of Physiology, School of Veterinary Medicine, Louisiana State University; Ph.D. awarded in May, 1998.
Dissertation: Interaction of Nitric Oxide and the Sympathetic Nervous System in the Control of Regional Vascular Resistance

MEMBERSHIPS IN SCIENTIFIC AND ACADEMIC SOCIETIES

American Association for the Advancement of Science
American Institute of Nutrition
American Physiological Society
North American Association for the Study of Obesity
Society for the Study of Ingestive Behavior

ACADEMIC HONORS AND AWARDS

1984 - 1986	NIH Individual Postdoctoral Fellowship Vassar College, Poughkeepsie, NY
1981	NSF Undergraduate Research Program Grant Co-sponsor with Stephen C. Woods, Ph.D. University of Washington, Seattle, WA
1980 - 1981	Graduate School Research Fund Grant Recipient (co-authored with Herman Samson, Ph.D.) Mechanisms of Satiety Hormones University of Washington, Seattle, WA
1977 - 1982	NIH Predoctoral Fellow University of Washington, Seattle, WA
1976	Bachelor of Science University of Washington, Seattle, WA Cum Laude and Phi Beta Kappa

NATIONAL PROFESSIONAL SERVICE

1997	Ad hoc member, NIH Special Study Section
1996	Ad hoc member, NIH Special Study Sections

Organizing Committee, 1998 Summer Faseb Conference on Behavioral and Metabolic Subphenotypes in Obesity

1995 Organizing Committee, Annual Meeting for the North American Association for the Study of Obesity

Ad hoc member, NIH Special Study Section

1994 - 1996 Education Committee, North American Association for the Study of Obesity

1993: Ad hoc member Nutrition Study Section
CNRU Site Visit Team, National Cancer Institute

INSTITUTIONAL SERVICE

1993 - 1997 Institutional Animal Care and Use Committee
Pennington Biomedical Research Center

1990 - 1991 Chairman, Curriculum Committee
Eastern Virginia Medical School

1989 - 1990 Member, Curriculum Committee
Eastern Virginia Medical School

1988 - 1991 Institutional Animal Care and Use Committee
Veterans Affairs Medical Center, Hampton, VA

AD HOC REVIEWER

American Journal of Physiology
Appetite
Genomics
International Journal of Obesity
Journal of Nutrition
Journal of Clinical Nutrition
Journal of Clinical Investigation
Mammalian Genome
Metabolism
Obesity Research
Peptides
Physiology & Behavior

Proceedings of the National Academy of Science

EDITORIAL BOARDS

American Journal of Physiology (1993)

INVITED PRESENTATIONS

2000: "Mouse Models and Functional Genomics". Invited speaker at the Jackson Laboratory/Roche Laboratory symposium on Functional Genomics of Diabetes And Obesity. Palo Alto, CA.

1999: "Complex Genetics of Obesity". Invited speaker at 1999 Neuroscience Festival at the University of Cincinnati, Cincinnati, OH

Panelist: "Dietary fat and obesity" 1999 meeting of the Society for Experimental Biology, Washington D.C.

"Congenic Lines and the Deconvolution of Complex Genetics". Invited seminar speaker at the University of Oregon Health Sciences Center, Department of Neurosciences, Portland, OR

"Mouse Genetics/Genomics for Target Identification and Validation". Invited Speaker at the annual winter conference on Medicinal and Bio-organic Chemistry, Park City, UT

1998: "Genetic Basis of High-Fat Induced Obesity". Presentation at the 8th International Congress on Obesity, Paris, France

"Obesity QTLs in Rodents". American College of Sports Medicine. Symposium on Obesity, Orlando, FL

"Man-Mouse Synteny: A Paradigm for Unraveling the Complexity of Human Genetic Disorders". March of Dimes Symposium on Complex Human Genetic Disorders. Los Angeles, CA

"Dietary Fat and Gene Interactions". Pennington Biomedical Research Center Symposium on "Nutrition, Genetics and Obesity", Baton Rouge, LA

1997: "Genetics of Obesity in Animal Models: Relevance to Obesity Associated Hypertension. Presented at 1997 Experimental Biology

Symposium on Obesity and Hypertension. New Orleans, LA

1996: "Genetics and Physiology of Dietary Obesity in the Mouse" presented to: Department of Clinical Nutrition, University of Texas Southwestern Medical School, Dallas TX

Smith Kline Beecham, Welwyn Garden City, England

School of Agriculture, University of Nebraska, Lincoln NB

Symposium on Genetics of Obesity in Animal Models, Experimental Biology 1996 Annual Meeting, Washington, D.C.

2nd International Conference on Oils and Disease, University of Texas Southwestern Medical School, Dallas TX

Sixth Benjamin Franklin Lafayette Seminar on Mechanisms of Food Intake and Specific Appetites, Sponsored by Cornell University, Pennsylvania State University, and College de France, La Napoule, France

Third International Symposium on Obesity and NIDDM, Sponsored by The Clore Laboratory at the University of Buckingham, Buckingham England

Department of Nutritional Sciences, University of Illinois, Champagne-Urbana, IL

Biology Section, Oakridge National Laboratory, Oakridge, TN

Psychology Department, Florida State University, Tallahassee FL

1995: FASEB Summer Research Conference on Genetic and Behavioral Influences on Nutrient Metabolism and Obesity, Copper Mountain, CO. "Molecular Genetics of Dietary Obesity in the Mouse"

NIH, NIDDK Conference on Prevention and Treatment of Childhood Obesity, Bethesda, MD. "Molecular Genetics: Implications for Pediatric Obesity Research"

Annual Meeting of the North American Association
for the Study of Obesity, Baton Rouge, LA. "Dietary
Fat and Obesity: Genetic Models of Obesity in Animals"

CME Course on the Prevention and Treatment of
Obesity in Special Populations, New Orleans, LA.
"Genetics/Environment is the Primary Determinant
of Most Cases of Obesity"

1994: Symposium on the Molecular and Genetic Aspects of
Obesity, Pennington Biomedical Research Center
Baton Rouge, Louisiana "Genetics of Dietary Obesity"

Seventh International Congress on Obesity
Toronto, Canada
Round Table Discussant; Prevention of Obesity

Obesity, Diabetes, and Insulin Resistance:
Implications from Molecular Biology, Epidemiology,
and Experimental Studies in Humans and Animals
American Diabetes Association
Boston, Massachusetts
"Dietary Obesity, Insulin Resistance, and Hypertension, A Canine Model"

Visiting Scientist, Jackson Laboratory,
Bar Harbor, Maine "Molecular Genetics of Dietary
Obesity in the Mouse"

1993: Division of Cardiology
Obesity Training Grant Speakers Program
University of California
Los Angeles, California
"Genetics of Dietary Obesity in the Mouse"

Department of Nutrition
University of California
Davis, California
"Genetics of Dietary Obesity in the Mouse"

First Department of Internal Medicine
Gunma University School of Medicine
Gunma, Japan

"Genetics and Physiology of Dietary Obesity in the Mouse"

1992: Continuing Medical Education
Emory University
Obesity Update: Pathophysiology, Clinical Consequences, and Therapeutic Options
"Hypertension and Obesity"

1991: Fifth Benjamin Franklin/Lafayette Symposium on the Physiology of Appetitive Behavior
La NaPoule, France
"Dietary Obesity in Mice"

1989: FASEB Summer Research Conference on Energy Metabolism.
Saxtons River, VT
"Adipose Tissue Blood Flow and Metabolism"

Annual meeting of the North American Association for the Study of Obesity
Washington, DC
"Animal Models of Obesity Associated Hypertension"

1988: Benjamin Franklin/Lafayette Symposium on the Physiology of Appetitive Behavior
La NaPoule, France
"Peptide Hormones and the Control of Food Intake"

Buckingham University
Symposium on Insulin and Obesity
Buckingham, England
"Regulation of Adipose Tissue Blood Flow by Insulin"

1987: Appetitive Seminar
Columbia University, New York, NY
"The Use of Short-acting Anorectic Agents for the Long-term Reduction of Food Intake"

Fifth Annual Virginia Nutrition Conference
"Role of Genetics and Adipocyte Development"

Harvard Medical School Continuing Education
Program on Treatment of Obesity: Diet,
Pharmacology, and Surgical Approaches
Cambridge, MA
"Cholecystokinin and Other Peptide Hormones"

1986: Department of Pharmacology
Hoffman La-Roche, Nutley, NJ
"Peptides and the Chronic Suppression of Food Intake"

Department of Psychology
State University of New York, Albany, NY
"Early Nutrition and the Development of Obesity"

Department of Nutrition
University of Georgia, Athens, GA
"Experimental Approaches in Animals to Study the Causes and Consequences of Obesity"

REFERENCES

Ron Krauss, M.D.
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Current Academic Department Head
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PUBLICATIONS

Iakoubova, O.A., Olsson, C.L., Dains, K.M., Choi, J., Kalcheva, I., Bentley, L.G., Cunanan, M., Hillman, D., Louie, J., Machrus, M. and West, D.B. Microsattellite marker panels for use in high-throughput genotyping of mouse crosses. In Press: *Physiological Genomics.*

Dhar M, LS Webb, L Smith, L Hauser, DKJohnson and DB West. A Heterozygous Deletion of a Novel ATPase Gene on Mouse Chromosome 7 Increases Body Fat. In Press: *Physiological Genomics*.

West DB, Y Ma, AA Truett, B York. Identification of Genes Involved in Animal Models of Obesity. *Handbood of Experimental Pharmacology: Obesity Pathology and Therapy*, Volume 149. D.H. Lockwood & T.G. Heffner (eds), Springer-Verlag, New York, pp 427-459, 2000.

West DB, FY Blohm, AA Truett, JP DeLany. Conjugated linoleic acid persistently increases total energy expenditure in AKR/J mice with no significant increase in uncoupling protein gene expression. J Nutr. 130(10): 2471-7, 2000.

Congenic Strains Confirm An Obesity Locus On Mouse Chromosome 4 Which Displays Regional Specificity and Epistatic Interactions. David B. West, James M. Cheverud, Alycia A. Truett, Tom Borges, Gary Truett and Barbara York Accepted with revisions by *Mammalian Genome*

Smith BK, PK Andrews and DB West. Macronutrient diet selection in thirteen mouse strains. Am J. Physiol. 278: R797-R805, 2000.

West DB, O Iakoubova, C Olsson, D Ross, J Ohmen & A Chatterjee. Mouse Genetics/Genomics: An effective approach for drug target discovery and validation. In Medicinal Research Reviews 20(3): 216-230, 2000.

York, B., and West, D.B. Polygenic models of rodent obesity. *Pennington Center Nutrition Series*: Volume 9. G.A. Bray & D.H. Ryan (Eds), Louisiana State University Press, Baton Rouge, pp 46-72, 1999.

Smith BK, PK Andrews, DA York, DB West. Divergence in proportional fat intake in AKR/J and SWR/J mice endures across diet paradigms. Am. J. Physiol. 277: R776-785, 1999.

York B, AA Truett, MP Monteiro, SJ Barry, CH Warden, JK Naggert, TP Maddatu, DB West. Gene-environment interaction: a significant diet-dependent obesity locus demonstrated in a congenic segment on mouse chromosome 7. Mammalian Genome 10: 457-462, 1999.

Delany JP, F Blohm, AA Truett, JA Scimeca, DB West. Conjugated linoleic acid rapidly reduced body fat content in mice without affecting energy intake. Am. J. Physiol. 276: R1172-R1179, 1999.

West DB & B York. Molecular genetics of dietary obesity in the mouse. In: Progress in Obesity Research, pp 145-149. J. Libbey and Company Ltd. London and New York, B Guy-Grand and G Ailhaud, eds. 1999.

Geiselman, P.J., Anderson, A.M., Dowdy, M.L., West, D.B., Redmann, S.M., and Smith, S.R. Reliability and validity of a macronutrient self-selection paradigm and a food preference questionnaire. *Physiology and Behavior*: 63: 919-928, 1998.

West, D.B., DeLany, J.P., Camet, P.M., Blohm, F., Truett, A.A., and Scimeca J. Effects of Conjugated linoleic acid on body fat and energy metabolism in the mouse. *Am J Physiol* 275: R667-R672, 1998.

West, D.B., and York, B. Dietary fat, genetic predisposition, and obesity: lessons from animal models. *Am J Clin Nutr* 67(Suppl 3): 505S-512S, 1998.

West.D.B., and York, B. Mouse models of human overweight. In: Human Polygenic Diseases, Dragani, T.A., Ed., Harwood Academic Publishers, pp 113-129, 1998

Truett A.A., Borne, A.T., Monteiro, M.P., and West, D.B. Composition of dietary fat affects blood pressure and insulin responses to dietary obesity in the dog. *Obesity Research* 6: 137-146, 1998.

Smith, B.K., West, D.B., and York, D.A. Carbohydrate vs fat intake: Differing Patterns of macronutrient selection in two inbred mouse strains. *Am J Physiol* 272: R357-R362, 1997.

York, B., Lei, K., and West, D.B. Inherited non-autosomal effects on body fat in F2 mice derived from an AKR/J x SWR/J cross. *Mammalian Genome* 8: 726-730, 1997.

West, D.B. Genetics of obesity in humans and animal models. *Endocrinology and Metabolism Clinics of North Am* 25: 801-813, 1996. Eds. G.A. Bray, Ed. W.B. Saunders Company, Philadelphia, PA.

Thompson, G.D. and West, D.B. Race and physical activity: cardiovascular and renal response to sodium loading. *Ethnicity and Disease* 6: 255-265, 1996.

York, B., Lei, K., West, D.B. Sensitivity to dietary obesity linked to a locus on chromosome 15 in a CAST/Ei x C57BL/6J F_2 intercross. *Mammalian Genome.* 7: 677-681, 1996.

Borne, A.T., Wolfsheimer, K.J., Truett, A.A., Kiene, J., Wojciechowski, T., Davenport, D.J., Ford, R.B., and West, D.B. Differential metabolic effects of energy restriction in dogs using diets varying in fat and fiber content. *Obesity Research* 4: 337-346, 1996.

West, D.B., York, B.A., Goudey-Lefevre, J., and Truett, G.E. Genetics and physiology of dietary obesity in the mouse, pp 100-119. In: *Pennington Center Nutrition Series, Vol 5: Molecular and Genetic Aspects of Obesity.* G.A. Bray and D. Ryan, Eds., Louisiana State University Press, Baton Rouge, 1996.

Truett, A.A., Borne, A.T., Poincot, M., and West, D.B. Autonomic control of blood pressure and heart rate in obese hypertensive dogs. *Am J Physiol* 270: R541-549, 1995.

West, D.B., Waguespack, J., and McCollister, S. Dietary obesity in the mouse: Interaction of strain with diet composition. *Am J Physiol* 268: R658-R665, 1995.

Truett, A.A. and West, D.B. Validation of a radio-telemetry system for continuous blood pressure and heart rate monitoring in dogs. *Lab Anim Sci* 45(3): 299-302, 1995.

West, D.B., Goudey-Lefevre, J., York, B.A. and Truett, G.E. Dietary obesity linked to genetic loci on chromosomes 9 and 15 in a polygenic mouse model. *J Clin Invest* 94: 1410-1416, 1994.

Eberhart, G.P., West, D.B. and Boozer, C.N. Insulin sensitivity of adipocytes from inbred mouse strains resistant or sensitive to dietary obesity. *Am J Physiol* 266: R1423-R1428, 1994.

West, D.B., Waguespack, J., York, B.A., Goudey-Lefevre, J. and Price, R.A. Genetics of dietary obesity in AKR/J x SWR/J mice: Segregation of the trait and identification of a linked locus on chromosome 4. *Mammalian Genome* 5: 546-552, 1994.

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Biomol Eng 2001 Jun;17(6):157-65

Co-expression of multiple transgenes in mouse CNS: a comparison of strategies.

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The introduction of two transgenes into one animal is increasingly common as transgenic experiments become more sophisticated. In this study we examine two strategies for creating double transgenic founders from a single microinjection. In the first approach, two constructs, each with its own promoter element, were coinjected into the pronucleus. In the second approach, both transgenes were cloned into one vector, separated by an internal ribosomal entry site (IRES), and placed under control of a single promoter. Both strategies save time and increase the percentage of double transgenic offspring over the standard method of mating single transgenic lines. However, despite high transgene copy numbers, the bicistronic lines did not show robust expression of either protein. Copy number and protein expression correlated much better in the coinjected lines, with expression levels in one line approaching that observed in some of our best single transgenic controls. Thus we recommend coinjection of individual plasmids for the generation of multiply transgenic founders.

PMID: 11337275 [PubMed - indexed for MEDLINE]